

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



10/532194



(43) International Publication Date
13 May 2004 (13.05.2004)

PCT

(10) International Publication Number
WO 2004/039811 A3

(51) International Patent Classification⁷: C07D 501/36

(21) International Application Number:
PCT/IN2003/000345

(22) International Filing Date: 27 October 2003 (27.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
937/MUM/2002 29 October 2002 (29.10.2002) IN

(71) Applicant (for all designated States except US): LUPIN LIMITED [IN/IN]; 159 CST Road, Kalina, Santacruz (East), Mumbai 400 098, Maharashtra (IN).

(72) Inventors; and

(75) Inventors/Applicants (for US only): TYAGI, Om, Dutt [IN/IN]; Lupin Limited (Research Park), 46A/47A, Nande Village, Taluka Mulshi, Pune 411 042, Maharashtra (IN). RICHHARIYA, Santosh, Kumar [IN/IN]; Lupin Limited (Research Park), 46A/47A, Nande Village, Taluka Mulshi, Pune 411 042, Maharashtra (IN). PAWAR, Rajesh, Kumar, Ramchandra [IN/IN]; Lupin Limited (Research Park), 46A/47A, Nande Village, Taluka Mulshi, Pune 411

042, Maharashtra (IN). CHAVAN, Yuvaraj, Atmaram [IN/IN]; Lupin Limited (Research Park), 46A/47A, Nande Village, Taluka Mulshi, Pune 411 042, Maharashtra (IN).

(74) Agents: SUBRAMANIAM, Hariharan et al.; Subramaniam, Nataraj & Associates, Patent & Trademark Attorneys, E-556, Greater Kailash-II, New Delhi 110 048 (IN).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

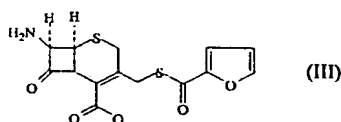
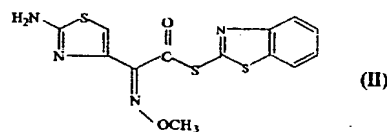
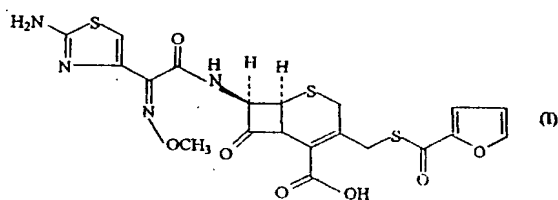
(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

[Continued on next page]

(54) Title: A METHOD FOR MANUFACTURE OF CEFTIOFUR



(57) Abstract: A process for preparation of ceftiofur of formula (I) of high purity and substantially free from impurities is disclosed. The process comprises reacting [2-(2-aminothiazol-4-yl)]-2-syn-methoxyimino acetic acid-2-benzothiazolyl thioester of formula (II), with 7-amino-3-(2-furanylcarbonylthiomethyl)-3-cephem-4-carboxylic acid of formula (III) in the presence of a mixture of an water-immiscible inert organic solvent and water and in the presence of a organic base and isolating ceftiofur of formula (I) substantially free of impurities by, d) adding water to the reaction mixture and selectively partitioning the impurities in the organic phase and ceftiofur (I) in the form of a salt with the base in the aqueous phase, e) acidifying the aqueous phase containing ceftiofur (I) in the form of a salt with the base in the presence of a mixture containing a water-miscible and a water-immiscible organic solvent and in the presence of a saturated aqueous solution of an alkali or alkaline earth containing salt, to partition ceftiofur (I) in the organic phase, and f) isolating ceftiofur (I) of high purity and substantially free of impurities by evaporation of the organic solvent or precipitation by addition of a co-solvent.

EXPRESS MAIL LABEL
NO.: EV 480459394 US



WO 2004/039811 A3